

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

Please add new claims 167-172.

1-122 (Cancelled)

123. (Currently amended) A method for promoting one or more of growth, differentiation, and survival of neuronal cells in culture, comprising contacting said cells with an amount of a *hedgehog* polypeptide comprising an amino acid sequence at least 80% identical to at least one sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal fragment of at least 50 contiguous amino acid residues thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of the *hedgehog* polypeptide is effective to promote one or more of growth, differentiation, and survival of said cells in culture.

124. (Currently amended) A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells in culture with an effective amount of a *hedgehog* polypeptide comprising an amino acid sequence at least 80% identical to at least one sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal fragment of at least 50 contiguous amino acid residues thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of the *hedgehog* polypeptide is effective to increase the survival of the neuronal cells in culture.

125. (Currently amended) A method for promoting growth, differentiation, or survival of mammalian ~~neuronal~~ neural stem cells in culture, comprising treating the cells with an amount of a *hedgehog* polypeptide comprising an amino acid sequence at least 80% identical to at least one sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal fragment of at least 50 contiguous amino acid residues thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein the amount

of the *hedgehog* polypeptide is effective to increase the rate of growth of the ~~neuronal~~ neural stem cells in culture.

126. (Previously added) The method of any one of claims 123, 124, or 125, wherein said *hedgehog* polypeptide is administered in combination with one or more other neurotrophic factors.

127. (Previously added) The method of claim 126, wherein said other neurotrophic factor is selected from CNTF, BDNF, and NGF.

128. (Previously added) The method of claim 123, wherein said neuronal cells are neural progenitor cells.

01 129. (Previously added) The method of claim 123, wherein said neuronal cells differentiates into cells having a selected neural phenotype.

130. (Previously added) The method of claim 129, wherein said neuronal cells differentiate into cells of the central nervous system or the peripheral nervous system.

131. (Cancelled)

132. (Cancelled)

133. (Currently amended) The method of any one of claims ~~claim~~ 123, 124, or 125, wherein said *hedgehog* polypeptide comprises an amino acid sequence identical to ~~with~~ an amino acid sequence designated in one of SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal fragment of at least 150 ~~50~~ contiguous amino acid residues thereof.

134. (Previously amended) The method of any one of claims 123, 124, or 125, wherein said *hedgehog* polypeptide has an amino acid sequence which is encoded by a nucleic acid which hybridizes under stringent conditions, including a wash step of $0.2 \times \text{SSC}$ at 65°C , to a nucleic acid sequence selected from SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6.

135. (Currently amended) The method of claim 123, wherein said *hedgehog* polypeptide comprises an amino acid sequence ~~is encoded by a nucleic acid which is~~ at least 98% identical with to at least one of a nucleic amino acid sequence designated in SEQ ID NO: 8 1, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of at least 150 contiguous nucleotides thereof.

136. (Currently amended) The method of claim 123, wherein said *hedgehog* polypeptide comprises an amino acid sequence ~~is encoded by a nucleic acid which is~~ at least 90% identical with to at least one of a nucleic amino acid sequence designated in SEQ ID NO: 8 1, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of at least 150 contiguous nucleotides thereof.

137. (Currently amended) The method of claim 123, wherein said *hedgehog* polypeptide comprises an amino acid sequence ~~is encoded by a nucleic acid which is~~ at least 95% identical with to at least one of a nucleic amino acid sequence designated in SEQ ID NO: 8 1, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of at least 150 contiguous nucleotides thereof.

138. (Currently amended) The method of any one of claims claim 123, 124, or 125, wherein said polypeptide includes a *hedgehog* amino acid sequence ~~at least 90 percent identical to~~ with a sequence selected from residues 104-189 of SEQ ID NO: 8, residues 102-187 of SEQ ID NO: 11, or residues 101-186 of SEQ ID NO: 12.

139. (Currently amended) The method of any one of claims claim 123, 124, or 125, wherein said polypeptide includes a *hedgehog* amino acid sequence ~~at least 90 percent identical to~~ with a sequence selected from residues 27-189 of SEQ ID NO: 8, residues 25-187 of SEQ ID NO: 11, or residues 24-186 of SEQ ID NO: 12.

140. (Currently amended) The method of any one of claims claim 123, 124, or 125, wherein said polypeptide includes a *hedgehog* amino acid sequence ~~at least 90 percent identical to~~ with an amino acid sequence selected from residues 27-425 of SEQ ID NO: 8, residues 25-437 of SEQ ID NO: 11, residues 24-418 of SEQ ID NO: 12, or residues 24-475 of SEQ ID NO: 13.

141. (Previously added) The method of claim 123, wherein said polypeptide includes an amino acid sequence encoded by a naturally occurring vertebrate *hedgehog* gene.

142. (Previously added) The method of claim 141, wherein said *hedgehog* gene is a mammalian *hedgehog* gene.

143. (Previously added) The method of claim 142, wherein said *hedgehog* gene is a human *hedgehog* gene.

144. (Currently amended) The method of any one of claims claim 123, 124, or 125, wherein said polypeptide includes an amino acid sequence which is encoded by at least a portion of a *hedgehog* gene of vertebrate origin selected from nucleotides 64-567 of SEQ ID NO: 1, nucleotides 73-561 of SEQ ID NO: 4, and nucleotides 70-558 of SEQ ID NO: 5.

01
145. (Cancelled)

146. (Previously added) The method of claim 123, wherein said polypeptide includes at least 150 contiguous amino acid residues of the N-terminal half of a *hedgehog* protein.

147. (Previously added) The method of claim 123, wherein said polypeptide binds to a naturally occurring *patched* receptor.

148. (Previously added) The method of claim 147, wherein said *patched* receptor is a patched receptor of a vertebrate organism.

149. (Previously added) The method of claim 123, wherein said neuronal cells are selected from motor neurons, cholinergic neurons, dopaminergic neurons, serotonergic neurons and peptidergic neurons.

150. (Cancelled)

151. **(Previously added)** The method of claim 123, wherein said polypeptide includes at least 50 contiguous amino acid residues of the N-terminal half of a *hedgehog* protein.

152. **(Previously added)** The method of claim 123, wherein said polypeptide includes at least 100 contiguous amino acid residues of the N-terminal half of a *hedgehog* protein.

01 153. **(Currently amended)** A method for promoting one or more of growth, differentiation, and survival of neuronal cells in culture, comprising contacting said cells with an amount of a *hedgehog* polypeptide encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in ~~one~~ any of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, ~~or an N-terminal fragment thereof of at least 150 contiguous nucleotides~~, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of a *hedgehog* polypeptide is effective to promote one or more of growth, differentiation, and survival of said cells in culture.

154. **(Currently amended)** A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells in culture with an amount of a *hedgehog* polypeptide effective to promote the survival of neuronal cells in culture, wherein said *hedgehog* polypeptide is encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in ~~one~~ any of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, ~~or an N-terminal fragment thereof of at least 150 contiguous nucleotides~~, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor.

155. **(Currently amended)** A method for promoting growth of mammalian ~~neuronal~~ neural stem cells in culture, comprising treating the cells with an amount of a *hedgehog* polypeptide ~~encoded~~ encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in ~~one~~ any of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, ~~or an N-terminal fragment thereof of at least 150 contiguous nucleotides~~, wherein said *hedgehog* polypeptide binds to a naturally

occurring *patched* receptor, and wherein said amount of a *hedgehog* polypeptide is effective to increase the rate of growth of the ~~neuronal~~ neural stem cells in culture.

156. (Currently amended) The method of claim 125, wherein said polypeptide sequence comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence which is at least 90% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 1, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 contiguous ~~nucleotides~~ thereof.

157. (Currently amended) The method of claim 125, wherein said polypeptide sequence comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence which is at least 95% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 1, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 contiguous ~~nucleotides~~ thereof.

01
158. (Currently amended) The method of claim 125, wherein said polypeptide sequence comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence which is at least 98% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 1, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 contiguous ~~nucleotides~~ thereof.

159. (Currently amended) The method of claim 124, wherein said polypeptide sequence comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence which is at least 90% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 1, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 contiguous ~~nucleotides~~ thereof.

160. (Currently amended) The method of claim 124, wherein said polypeptide sequence comprises a ~~polypeptide encoded by a nucleic acid~~ an amino acid sequence which is at least 95% identical to a ~~nucleic acid~~ an amino acid sequence designated in one of SEQ ID NO: 8 1, SEQ ID NO: 11 4, SEQ ID NO: 12 5, SEQ ID NO: 13 6, or an N-terminal auto-proteolytic fragment of 150 contiguous ~~nucleotides~~ thereof.

161. **(Currently amended)** The method of claim 124, wherein said polypeptide sequence comprises ~~a polypeptide encoded by a nucleic acid sequence~~ an amino acid sequence which is at least 98% identical to ~~a nucleic acid sequence~~ an amino acid sequence designated in one of SEQ ID NO: ~~8~~ 11, SEQ ID NO: ~~11~~ 4, SEQ ID NO: ~~12~~ 5, SEQ ID NO: ~~13~~ 6, or an N-terminal auto-proteolytic fragment of ~~150~~ contiguous nucleotides thereof.

162. **(Previously added)** The method of claim 123, wherein the N-terminal fragment is approximately 19 kD.

163. **(Previously added)** The method of claim 124, wherein the N-terminal fragment is approximately 19 kD.

164. **(Previously added)** The method of claim 125, wherein the N-terminal fragment is approximately 19 kD.

01 165. **(Currently amended)** The method of claim ~~128~~ 123, wherein said neural progenitor ~~neuronal~~ cells differentiate into glial cells.

166. **(Currently amended)** The method of claim ~~125~~ 129, wherein said ~~neuronal~~ neural stem cells differentiate into glial cells.

167. **(New)** The method of claim 123, wherein said polypeptide comprises an amino acid sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof.

168. **(New)** The method of claim 124, wherein said polypeptide comprises an amino acid sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof.

169. **(New)** The method of claim 125, wherein said polypeptide comprises an amino acid sequence selected from SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof.

170. (New) A method for promoting one or more of growth, differentiation, and survival of neuronal cells in culture, comprising contacting said cells with an amount of a *hedgehog* polypeptide comprising an amino acid sequence identical to an amino acid sequence designated in any of SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of the *hedgehog* polypeptide is effective to promote one or more of growth, differentiation, and survival of said cells in culture.

01 171. (New) A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells in culture with an effective amount of a *hedgehog* polypeptide comprising an amino acid sequence identical to an amino acid sequence designated in any of SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein said amount of the *hedgehog* polypeptide is effective to increase the survival of the neuronal cells in culture.

172. (New) A method for promoting growth, differentiation, or survival of mammalian neural stem cells in culture, comprising treating the cells with an amount of a *hedgehog* polypeptide comprising an amino acid sequence identical to an amino acid sequence designated in any of SEQ ID NO: 8, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, or an N-terminal auto-proteolytic fragment thereof, wherein said *hedgehog* polypeptide binds to a naturally occurring *patched* receptor, and wherein the amount of the *hedgehog* polypeptide is effective to increase the rate of growth of the neural stem cells in culture.
